

CLAIMS

1. An *in vitro* method that comprises:

- 5 a) the detection and/or quantification of the FGFR3 protein, of the mRNA of the *FGFR3* gene, or of the corresponding cDNA in a sample of an individual, and
- b) the comparison of the amount of FGFR3 protein, of the mRNA of the *FGFR3* gene or of the corresponding cDNA detected in a sample of an individual, with their normal reference values.

10 2. An *in vitro* method according to claim 1 which is employed to detect the presence of the bladder transitional cell carcinoma in an individual, to determine the stage or severity of this cancer in an individual or to monitor the effect of the therapy administered to the individual with this cancer.

15 3. Method according to claims 1 and 2 in which the sample to be analysed is a sample of bladder tissue.

 4. Method according to claim 3 in which the sample of bladder tissue is obtained by any conventional method, preferably by cystoscopy.

20 5. Method according to claims 1 and 2 in which the sample to be analysed is a sample of urine, blood, plasma, pleural fluid, ascitic fluid, synovial fluid, bile, semen or cerebrospinal fluid.

25 6. Method according to claims 1 and 2 in which the sample to be analysed is obtained from an individual not previously diagnosed with bladder transitional cell carcinoma.

30 7. Method according to claims 1 and 2 in which the sample to be analysed is obtained from an individual who has been previously diagnosed with bladder transitional cell carcinoma.

35 8. Method according to claims 1 and 2 in which the sample to be analysed is obtained from an individual receiving treatment, or who has been treated previously against bladder transitional cell carcinoma.

9. Method according to claims 1 and 2 characterised in that it comprises the extraction of the sample, either to obtain an extract of proteins or an extract of total RNA.

5 10. Method according to claim 1 characterised in that the detection and/or quantification of the FGFR3 protein comprises a first step, in which the protein extract of the sample is placed in contact with a composition of one or more specific antibodies, against one or more epitopes of the FGFR3 protein, and a second step, in which the complexes formed by the antibodies and the FGFR3 protein are quantified.

10 11. Method according to claim 10, characterised in that said antibodies correspond to monoclonal or polyclonal antibodies, intact or recombinant fragments of antibodies, combibodies and Fab or scFv antibody fragments, specific against the FGFR3 protein; these antibodies being human, humanised or of non-human origin.

15 12. Method according to claims 10 or 11 characterised in that in the detection and/or quantification of the complexes formed by antibodies and the FGFR3 protein, the techniques used are selected from the group comprised by: western-blot, ELISA (Enzyme-Linked Immunosorbent assay), RIA (Radioimmunoassay), Competitive EIA (Competitive Enzyme Immunoassay), DAS-ELISA (Double Antibody Sandwich-ELISA),
20 immunocytochemical or immunohistochemical techniques, techniques based on the use of biochips or protein microarrays that include specific antibodies, assays based on the precipitation of colloidal gold in formats such as dipsticks; or by affinity chromatography techniques, ligand binding assays or lectin binding assays.

25 13. Method according to claim 1 characterised in that the detection and/or quantification either of the mRNA or of the corresponding cDNA of the *FGFR3* gene, comprises a first step of amplification of the mRNA that is present in the extract of total RNA, or of the corresponding cDNA synthesised by reverse transcription of the mRNA; and a second step of quantification of the amplification product from either the mRNA or the
30 cDNA of the *FGFR3* gene.

14. Method according to claim 13 characterised in that the amplification is performed qualitatively or quantitatively, by RT-PCR using primer oligonucleotides, where the sequences of the primers used to amplify the sequence of the *FGFR3* gene are SEQ ID
35 NO.1 and SEQ ID NO.2.

15. Method according to claim 1 characterised in that the detection and/or quantification is done with specific probes either of mRNA or of the corresponding cDNA of the *FGFR3* gene, by techniques such as northern-blot or northern transfer.

5 16. Method according to claim 1 characterised in that the detection and/or quantification of the mRNA is done by Real time quantitative RT-PCR (Q-PCR).

10 17. Use of nucleotide or peptide sequences derived from the *FGFR3* gene, to detect *in vitro* the presence of a bladder transitional cell carcinoma, to determine *in vitro* the stage or severity of this cancer in the individual, or to monitor *in vitro* the effect of the therapy administered to an individual with this cancer.

18. An *in vitro* method to identify and evaluate the efficacy of therapeutic compounds against cancer bladder transitional cell carcinoma that comprises:

- 15 a) placing in contact a culture of bladder tumour cells (with uncontrolled proliferation) with the candidate compound, in the appropriate conditions and for a suitable time for these to interact,
- b) detect and/or quantifying expression levels of the *FGFR3* gene or the FGFR3 protein, and
- 20 c) compare said expression levels with those of the control cultures of tumour cells not treated with the candidate compound.

25 19. Use of a nucleotide or peptide sequence derived from the *FGFR3* gene, in methods to screen for, identify, develop and evaluate the efficiency of compounds to bladder transitional cell carcinoma.

20. An agent that inhibits the expression and/or activity of the FGFR3 protein.

30 21. An agent according to claim 20 selected from the group formed by:

- a) an antibody, or combination of antibodies, specific against one or more epitopes present in the FGFR3 protein, preferably a human or humanised monoclonal antibody; a fragment of an antibody, a single chain antibody or an anti-idiotypic antibody,
- 35 b) cytotoxic agents such as toxins, molecules with radioactive atoms or chemotherapeutic agents, including small organic and inorganic molecules, peptides, phosphopeptides, antisense molecules, ribozymes, triple helix

molecules, double stranded RNA etc., which inhibit expression and/or activity of the FGFR3 protein and

- c) antagonistic compounds of the FGFR3 protein, which inhibit one or more of the functions of the FGFR3 protein.

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22. Agent according to claims 20 or 21 to treat a cancer of the bladder transitional cell carcinoma.

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23. Use of any of the agents according to claims 20 or 21 in the manufacturing of a medicinal product for the treatment of bladder transitional cell carcinoma.

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24. Pharmaceutical composition comprising a therapeutically effective amount of at least one agent according to claims 20 or 21 and at least one pharmaceutically acceptable excipient.

25. Pharmaceutical composition according to claim 24 that characterised because it contains further active ingredients, preferably one that inhibits the function of the FGFR3 protein.

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26. A kit that comprises an antibody that specifically recognises the FGFR3 protein and a carrier in suitable packaging

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27. A kit that comprises a primer pair designed to specifically amplify a nucleic acid having a sequence that is specific to the *FGFR3* gene.

28. A kit according to claim 27 wherein the sequence of the primer pair is selected from SEQ ID NO.1 and SEQ ID NO. 2.

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29. A kit according to claims 26 to 28 that is employed to detect the presence of the bladder transitional cell carcinoma in an individual, to determine the stage or severity of this cancer in an individual or to monitor the effect of the therapy administered to the individual with this cancer.

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